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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/359,260
Filing Date: July 22, 1999
Appellant(s): CAMPBELL ET AL.

Leonid D. Thenor
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 09/04/2007 appealing from the Office action mailed 09/04/2007.

(1) Real Party in Interest

The statement of the Real Party in Interest contained in the Brief is correct.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief, filed 09/04/2007, is incorrect. The correct status of the claim is as follows:

Claims 1-75, 77-81, 91, 96-130, and 133 are cancelled.

Claims 76, 82-90, 92-95, 131, 132, and 134-138 are pending and on appeal.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is incorrect.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

Claims 76, 82, 87-90, 92-95, 131, 132, and 134-138 are rejected under 35 USC §102(b) as being anticipated by Ostrem et al.

Claims 76, 82-90, 92-95, 131, and 134-138 are rejected under 35 UC §103(a) as being unpatentable over Ostrem et al. in view of Cramer et al.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Ostrem et al. "Discovery of a Novel, Potent, and Specific Family of Factor Xa Inhibitors via Combinatorial Chemistry", Biochemistry (1998) Vol. 37, pages 1053-1059.

US Patent No. 6,240,374 Cramer et al. 05-2001

(9) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 76, 82, 87-90, 92-95, 131, 132, and 134-138 are rejected under 35 U.S.C. 102(b) as being anticipated by Ostrem et al.

[Claims 94, 95, 132, 134, 135, 137, and 138]: Ostrem et al. sets forth a procedure for drug discovery by the preparation of a octamer combinatorial test peptide library in order to identify leads compounds therein, which reads on the claimed limitation of identifying a predetermined set of peptides (see Ostrem et al., Abstract and page 1054, column 1, first paragraph). The library set forth in Ostrem et al. comprises peptides of 8 amino acids in length comprising a specific tripeptide sequence (second parameter) and have been evaluated as having a potency of 4 to 15 □M and retain an unusual selectively for factor Xa over thrombin (a first parameter), which reads on the instantly claimed determination of a first whole molecule parameter and a second parameter that is dependent on the specific order of constitutive subunits.
Ostrem et al. discloses the construction of a combinatorial library containing a multitude of varying peptide sequences in order to identify those specific sequences that have an enhanced activity, and as such provides a space-filling design wherein variations of octamer peptides have been explored in the both a sequence-space and conformational-space context (see Ostrem et al., at least Abstract and page 1053,

column 1, line 1 through column 2, line 32). The large number of varying peptide sequences in a peptide library are certainly "space-filling" elements, and the applied combinatorial approach used to construct a significant sampling of alternative peptide sequences is considered a "design". Therefore the construction of peptide libraries using a combinatorial approach, as taught by Ostrem et al., reads on the claimed limitation of constructing a first test peptide library comprising a plurality of first test peptides identified using a space-filling design.

Further, Ostrem et al. teaches that peptides in a library have the measurable property of binding factor Xa and inhibiting factor Xa activity, which reads on the claimed step of measuring the indicia of an activity of a plurality of first test peptides (see Ostrem et al. Abstract and page 1053, column 2, lines 23-32). The described procedures for testing a family of combinatorial peptides of 8 amino acids in length to bind factor Xa and level of potency reads on the claimed determination of a relationship between an indicia of activity, a first parameter, and a second parameter (see Ostrem et al., page 1054, column 1, line 1 through page 1055 column 1, line 41). Ostrem et al. further sets forth four separate assays that are described and performed on peptides identified from an initial set of combinatorial octamer peptides, wherein peptide-bound beads are separately prepared and used in each of the four distinct assays (see Ostrem et al., page 1054, column 2, line 1 through page 1055, column 1, line 41), which reads on the recited selecting, measuring, and identifying steps for a second test peptide library. Ostrem et al. further discloses the testing of a separate library of octamer peptides comprising C-terminal p-nitroanilide (pNA) substrates and isomeric forms (D-

forms) of the amino acid tripeptide repeats used in the original combinatorial peptide library (see Ostrem et al., Figures 2 and 3 and page 1056 col. 1, line 1 through col. 2, line 2), which also reads on the recited selecting, measuring, and identifying steps for a second test peptide library. The disclosed selection of peptides based on the results of these assays reads on the instantly claimed limitations of setting a test requirement having a test indicia range, selecting a second test peptide library different from said first test peptide library, measuring the indicia of each second test peptide, and identifying at least one second test peptide having a measured indicia that satisfies said test requirement.

Ostrem et al. further discloses that all peptides containing Tyr-Ile-Arg or Phe-ILe-Arg inhibited factor Xa activity in a prothrombin assay (see Ostrem et al., page 1055, col. 1, line 42 through col. 2, line 21). Further, resultant inhibition of factor Xa activity is shown in Figure 1 (see Ostrem et al., page 1055), which includes values of inhibition activity measured at several peptide concentrations and the calculation of sigmoidal curves that are fit to the measured factor Xa inhibition values. The calculation of these sigmoidal curves is based on the measured Xa inhibition values and are used to extrapolate the inhibition of peptides over concentrations ranges which were not directly measured and, therefore, teaches the derivation of a quantitative relationship between the measured indicia (factor Xa inhibition), the first parameter (octamers having a potency of 4 to 15 □M and retaining an unusual selectively for factor Xa over thrombin), and the second parameter (octamers comprising a specific tri-peptide sequence) as instantly claimed.

[Claim 76]: Evaluating the potency of the octamer combinatorial peptides set forth by Ostrem et al. sets forth a determination that the potency is a function of peptide sequence composition, which reads on the claimed limitation of determining a relationship comprising the step of determining $y_i=f(x_{ij})$, wherein potency is the whole molecule parameter X_{ij}, i represents the number representative of octamer peptide tested, j ranges from 1 to d, and d is 1 as only one whole molecule parameter is evaluated, and y_i represents potency, wherein the activity is determined for each octamer combinatorial peptide.

[Claim 82]: Ostrem et al. discloses the identification of a subset of peptides from an initial peptide library (comprising the tripeptide sequence of Tyr-Ile-Arg or Phe-ILe-Arg) that demonstrate an increased ability to bind factor Xa (see Ostrem et al., page 1055, col. 1, line 42 through col. 2, line 21), which reads on constituents of a first test peptide as recited in the instant claim. Ostrem et al further teaches the identified subset of peptides is further used in a prothrombin assay that tests for inhibition of factor Xa activity (see also Ostrem et al., page 1055), which reads on the recited space-filling design expanding less than all of the first test peptides into their constituents.

[Claims 87-90, 92, and 93]: Ostrem et al. teaches that factor Xa is an enzyme in the hemostasis pathway and acts as a receptor in the prothrombin complex with factor Va and calcium ion on a phospholipid surface (see Ostrem et al. page 1053, col. 1, line 1-23), which reads on the recited activity of binding to a receptor. Ostrem et al. further discloses the use of identified peptides in a prothrombin assay that tests for any enhancement or inhibition of factor Xa activity (see Ostrem et al., page 1055, col. 1, line

42 through col. 2, line 21) and additional *in vivo* assays comprising injection of specific peptides into rats and rabbits (see Ostrem et al., page 1057, col. 1, line 19 through col. 2, line 2), which reads on the recited limitations of inducement or inhibition of a biological activity in a cell.

[Claim 131]: Page 39, lines 7-34 of instant specification provides an exemplary embodiment of using a space-filling design wherein a particular cut-off distance for potential lead-compounds is used to identify compounds of interest. Further, it is reiterated that the combinatorial approach disclosed by Ostrem et al., used to construct a peptide library reads on the construction of a test peptide library using a space-filling design as instantly claimed. In said exemplary embodiment, the "distance function" that was applied was an arbitrary cut-off limit for the variability of the specific characteristics of peptide hydrophobicity and total dipole moment. Figure 4, Table 2, and pages 1056, line 1 through page 1057, column 2, line 2 of Ostrem et al. sets forth that identification of lead compounds comes from assessing estimated values of relative activity, protein concentration, and inhibition. Further, Figure 5 and page 1057, column 2, line 4 through page 1058, column 2, line 5 of Ostrem et al. discusses the criteria that were used to distinguish and identify novel lead compounds from amongst all compounds utilized in the investigation, which reads on the application of a distance function and is consonant with the above described example provided in the instant specification. Therefore, the above described method of identifying novel ligands by Ostrem et al. reads on the claimed limitation of a space-filling design that applies a distance function.

[Claim 136]: Page 45, lines 6 and 7 of the instant specification defines the claimed term "compound isomers" as "the group of compounds sharing common global characteristics". Ostrem et al. further discloses the testing of a separate library of octamer peptide comprising C-terminal p-nitroanilide (pNA) substrates and isomeric forms (D-forms) of the amino acid tripeptide repeats used in the original combinatorial peptide library (see Ostrem et al., Figures 2 and 3 and page 1056 col. 1, line 1 through col. 2, line 2), which reads on the instantly claimed steps of expanding first test peptides into their compound isomers and performing a space-filling design on said constituent compound isomers to identify candidate peptides.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 76, 82-90, 92-95, 131, 132, and 134-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ostrem et al. in view of Cramer (US Patent No 6,240,374).

[Claims 83-86]: As discussed above, Ostrem et al. sets forth a procedure for drug discovery by the preparation of a octamer combinatorial test peptide library in order to identify lead compounds therein. However Ostrem et al. does not teach the parameterization of a predetermined set of peptides using a first and second parameter selected from the groups recited in instant claims 83-86.

Cramer et al. sets forth a method of validating molecular structural descriptors that may be used to select optimally diverse subsets of molecules with a desired set of characteristics. See Cramer et al., Abstract. Cramer et al. further discloses an example wherein a library database of compounds is selected on the basis of molecular weight and hydrophobicity (see column 62, lines 38-50).

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to parameterize peptides on the basis of molecular weight and hydrophobicity, as taught by Cramer, in the procedure for drug discovery as set forth by Ostrem et al. where the motivation to do so is found in Cramer et al., who teaches that the optimizing the characteristics of compound libraries utilized in drug discover is critical for establishing a sufficiently diverse but manageable set of starting compounds for further investigation (see Cramer, column 2, lines 51 through column 3, line 67).

(10) Response to Argument

In regard to the rejection of claims under 35 USC 102(b) as being anticipated by Ostrem et al., appellant argues that Ostrem itself discloses that complete representation of peptides in the library was not known as only a select few peptides were confirmed as being available after activity assays were completed (see page 21, line 9-23 of the brief). Appellant further argues that Ostrem's library is necessarily biased toward factor Xa inhibitors and clearly is not representative of the entire octamer peptide space and

there is nothing in Ostrem to indicate that an attempt was being made to represent the entire octamer peptide space (see page 24, lines 3-23 of the brief).

In response to appellant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which appellant relies (i.e., representation of an entire octamer peptide space) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Appellant further argues that Ostrem fails to construct a first test peptide library designed to provide any organized representation of, for example, the total octamer space, mention a space-filling design, or provide some suggestion for a design that selects representatives from a plurality of compound isomers (see page 25, lines 1-14 of the brief). Appellant further argues that another indication that the complete set of peptides in Ostrem's library screening procedure was not known is the "split-synthesis" methodology used to generate the peptides and, further that Ostrem's selection of the split-synthesis method clearly supports the fact that a space-filling design was not applied (see page 22, lines 1-10 and page 25, lines 15-23 of the brief).

In response to arguments about a space filling design, it is reiterated that the instant claims do not recite any limitation requiring the construction of an exhaustively complete space obtained by the use of a space-filling design. Further, it is noted that page 19, lines 15-23 of the instant specification teaches that the term "space-filling

design" is "intended to be construed broadly and includes all such techniques known to those skilled in the art" (see especially page 19, lines 17-19) and further provides a listing of exemplary embodiments including maximum diversity libraries, coverage designs, cluster based designs, and any other optimal designs (see especially page 19, lines 19-23). As such, applicants' arguments that that Ostrem's library is necessarily biased toward factor Xa inhibitors and does not encompass the entirety of octamer peptide space is not persuasive because neither the instant claims nor specification define a space-filling design which must exhaustively encompass all possible regions within a defined "space". Ostrem et al. discloses the application of a combinatorial chemistry approach that relies upon sets of octamer peptides containing the minimal inhibitory tripeptide sequence, such as octamer peptides comprising the tripeptide sequence of L-tyrosinyl-L-isoleucyl-L-arginyl, in order to identify those peptides having an increased activity for inhibiting factor Xa (see Ostrem et al., at least Abstract and page 1053, column 1, line 1 through column 2, line 32). Therefore, contrary to appellant's argument, Ostrem et al. provides a space-filling design wherein a plurality of octamer peptides are produced by use of a combinatorial chemistry approach.

Appellant further argues that the only measurements taken by Ostrem appear to relate to the potency of the peptides and this value is different from the first and second parameters measured in the claimed invention (see page 22, lines 11-14 of the brief). Appellant further argues that there is no factual disclosure in Ostrem to support

parameterizing the predetermined set of peptides as recited in the claimed invention (see page 23, lines 13 through page 24, line 2 of the brief).

In response, it is first noted that the instant claims recite the limitations “the first parameter is a whole molecule parameter” and “the second parameter is dependent upon the specific order of constitutive subunits within each predetermined peptide”. Ostrem et al. discloses that each octamer peptide has a potency of 4 to 15 □M and retains an unusual selectively for factor Xa over thrombin, which reads on a first parameter that is a whole molecule parameter. Ostrem et al. further discloses that each octamer peptide comprises the tripeptide sequence of L-tyrosinyl-L-isoleucyl-L-arginyl, which reads on a parameter that is dependent upon the specific order of constitutive subunits as recited in the instant claims. It is further noted that the instant claims recite the limitations of “determining an activity, having an indicia” and “measuring the indicia of activity" for peptides within a fist and second library. Ostrem et al. discloses that the octamer peptides have the measurable property of binding factor Xa and further sets forth the assays used to measure this property, which reads on determining an activity having an indicia and measuring the indicia of activity as recited in the instant claims.

Appellant further argues that Ostrem measures the increased potency range of the initial leads identified in the combinatorial library and that they are not calculated from a derived relationship (see page 22, lines 14-16 of the brief). Appellant further argues that Ostrem merely measures quantities such as the inhibition of Xa activity and plots them in various graphs but does not contain a single quantitative formula that is

representative of these graphs (see page 26, lines 8-10 of the brief). Appellant further argues that Ostrem provides no disclosure or suggestion for deriving a quantitative relationship between the measured indicia, the first parameter, and the second parameter, since these parameters are not measured (see page 26, lines 1-8; page 26, line 22 through page 27, line 10; page 28, line 22 through page 29, line 14; and page 30, line 5 through page 34, line 13 of the brief). Appellant further asserts that his particular feature was discussed during the interview of June 20, 2005 wherein the Examiner agreed that this feature was not disclosed by Ostrem (see especially page 29, lines 4-7 of the brief).

In response, the inhibition of factor Xa activity is shown in Figure 1 (see Ostrem et al., page 1055), which includes measured values of inhibition activity and calculated sigmoidal curves that are fit to the measured factor Xa inhibition values. The calculation of these sigmoidal curves is based on the measured Xa inhibition values and are used to extrapolate the predicted inhibition of peptides at concentrations that were not directly measured and, therefore, teaches the derivation of a quantitative relationship between the measured indicia (factor Xa inhibition), the first parameter (octamers having a potency of 4 to 15 μM and retaining an unusual selectively for factor Xa over thrombin), and the second parameter (octamers comprising a specific tri-peptide sequence) as instantly claimed. Further, in response to applicants assertion that the Examiner agreed that this feature was not disclosed by Ostrem et al., during the interview of June 20, 2005, the interview summary of record (a copy of which was provided to applicants on 06/20/2005) clearly indicates that no agreement was reached with respect to the claims.

Appellant further argues that Ostrem simply fails to enable the claimed invention (see page 23, lines 8-12 and page 29, lines 14-18 of the brief). Appellant further argues that Ostrem's failure to disclose specific features recited in the claims are at issue because the anticipatory reference is required to enable the claimed invention against which it is being applied, that the validity of Ostrem's result's have never been questioned or challenged, and it is not necessary to provide any factual evidence challenging the validity of Ostrem's procedures and results since they clearly differ from the claimed invention (see page 22, line 22 through page 23, line 7 of the brief). Appellant further argues that Ostrem cannot be considered enabling because the initial selected peptides failed to perform in their intended *in vivo* application and the core motif required further modification to yield a functional peptide (see page 29, line 19 through page 30, line 4 of the brief).

In response, it is first noted that MPEP § 2121 states that when a reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980) (see also MPEP § 716.07). Further, while appellant argues that it is not necessary to provide any factual evidence challenging the validity of Ostrem's procedures and results, appellant argues that Ostrem cannot be considered enabling because the initial selected peptides failed to perform in their intended *in vivo* application. This argument is not persuasive because Ostrem et al. is directed to a screening method for identifying low molecular weight

peptide inhibitors of factor Xa. It is also emphasized that Ostrem et al. discloses several successful applications of the disclosed method wherein screened peptides where identified as having a "desired activity", i.e. effective low molecular weight peptide inhibitors of factor Xa (Tables 1 and 2, Figures 1 and 2, and page 1055, column 1, line 43 through page 1057, column 2, line 2). Further, the instant claims do not recite any *in vivo* limitations, nor any limitations with regard to potential drug products, nor any limitations with regard to pharmacological or pharmaceutical activity. The successful application of Ostrem et al.'s disclosed screening method is not invalidated by the results obtained from the additional *in vivo* applications (see Ostrem et al., page 1057, col. 1, line 19 through col. 2, line 2). Ostrem et al. discloses all experimental procedures relied upon in the experimental assays as well as several additional references further describing the experimental protocols (see Ostrem et al., page 1054, column 1, line 1 through page 1055, column 1, line 41).

Appellant further argues that it is difficult to see how Ostrem could have used peptides attached to a synthesis resin in a screen for peptides intended to enhance culture media and to the development of a process for enhancing culture media (see page 26, lines 11-21 of the brief).

In response, it is noted the invention elected in response to the original restriction requirement (mailed 09/12/2000) is drawn to a method of identifying peptides with a predicted indicia of activity (Group VII) (see applicants' response to the restriction requirement filed 10/12/2000). Therefore appellant's argument directed to a screen for

peptides intended to enhance culture media and to the development of a process for enhancing culture media is not germane because it is directed to a non-elected invention (see Groups I, IV, V, VIII, and IX of the original restriction requirement mailed 09/12/2000).

Appellant further argues that the examiner uses hindsight to misconstrue the teachings of Ostrem to read on the claimed invention (see page 26, lines 10-12 of the brief). Appellant further argues that the examiner states that Ostrem performs four separate assays wherein peptide-bound beads are separately prepared and used in each of the four distinct assays and that this analogy appears contrary to the claimed steps and teaches away from the present invention (see page 27, line 12 through page 28, line 8 of the brief).

In response, it is first noted that the instant rejection is one of anticipation set forth under 35 US 102(b) and as such the arguments that the examiner's conclusion is based upon improper hindsight reasoning and that the Ostrem et al. teaches away from the claimed invention are not germane. However, it is acknowledged that the instant claim is further included the rejection under 35 USC 103(a) as being unpatentable over Ostrem et al. in view of Cramer et al. In regard to conclusions based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d

1392, 170 USPQ 209 (CCPA 1971). On this point, it is emphasized that the basis of the instant rejection under 35 USC 103(a) relies only upon the teachings set forth in the prior art and does not does not include knowledge gleaned only from the applicant's disclosure. Further, appellant's argument that the disclosure of Ostrem et al., regarding separate assays performed on distinct sets of peptides, teaches away from the present invention is not persuasive because independent claims 135-138, in fact, require separate assays performed on distinct sets of peptides (see especially claim 135, which recites measuring indicia for a plurality of a first test peptides as step six, then recites a separate step (step 11) of measuring the indicia of each second test peptide).

Appellant further argues that the estimated indicia [of the claimed invention] is calculated for peptides that remain from a predetermined set of peptides which are not included from the first test peptide library and have not yet been tested and, in contrast, Ostrem never goes outside the original combinatorial library to identify peptides that have not been assayed and calculate an estimated value for the inhibition factor Xa activity prior to performing an assay (see page 28, lines 9-16 of the brief).

Appellant's argument that Ostrem never goes outside the original combinatorial library is incorrect. Ostrem et al. explicitly teaches the use of a separate library of octamer peptides comprising C-terminal p-nitroanilide (pNA) substrates and isomeric forms (D-forms) of the amino acid tripeptide repeats that were derived from the original combinatorial peptide library (see Ostrem et al., Figures 2 and 3 and page 1056 col. 1, line 1 through col. 2, line 2).

In regard to the rejection of claim 135 under 35 USC 103(a) as being unpatentable over Ostrem et al. in view of Cramer et al., appellant argues that Cramer et al. does nothing to remedy the shortcomings of Ostrem (see Page 38, lines 10-13 of the brief). In regard claims 136-138 under 35 USC 103(a) as being unpatentable over Ostrem et al. in view of Cramer et al., appellant reiterates the text of claims 136-138 and argues that the Examiner does not raise any new grounds for rejection against the instant claims. Appellant further argues that the combination of Ostrem and Cramer fails to render independent claim 136 obvious since various claim features are neither disclosed nor discussed (see page 39, line 17 through page 43, line 13).

In response, the arguments regarding alleged shortcomings of Ostrem et al. have been addressed above.

Appellant further argues that Cramer does not even appear to disclose or suggest the features recited in claims 83-86 (see page 38, lines 13 and 14 of the brief). Appellant further argues that Cramer is not concerned with the screening of peptides and/or determination of desired activities (see page 38, lines 14-24 of the brief). Appellant further argues that neither the combination nor individual references teaches a method for identifying peptides having a desired activity (see page 39, lines 4-9 of the brief).

In response, it is reiterated from the instant rejection that Cramer et al. sets forth a method of validating molecular structural descriptors that may be used to select

optimally diverse subsets of molecules with a desired set of characteristics (see Cramer et al., Abstract), and is directly related to the selection of a comprehensive peptide library as applied in Ostrem et al. Cramer et al. further discloses examples wherein a library database of compounds is selected on the basis of molecular weight and hydrophobicity (see column 62, lines 38-50), which, contrary to appellants argument, reads on alternative embodiments recited in instant claims 83-86. The screening of a combinatorial peptide library for novel, potent, and specific factor Xa inhibitors, as taught by Ostrem et al., reads directly on a method for identifying peptides having a desired activity.

Appellant further argues that Ostrem and Cramer do not even appear to be properly combinable because neither reference provides any motivation to seek out the teachings of the other with a realistic expectation of arriving at the claimed invention (see page 38, line 24 through page 39, line 3 of the brief).

In response, it is reiterated from the rejection above that the motivation to combine the teachings of Ostrem et al. and Cramer et al. is the express teaching from Cramer et al. that optimizing the characteristics of compound libraries utilized in drug discover is critical for establishing a sufficiently diverse but manageable set of starting compounds for further investigation (see Cramer, column 2, lines 51 through column 3, line 67). Therefore, appellants argument that neither reference provides any motivation to seek out the teachings of the other is incorrect and unpersuasive.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Conclusion

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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